

Appl. No. : Not yet assigned
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IN THE CLAIMS:

Please cancel all the pending claims 1-41.

Please add the following new claims 42-76:

42. (NEW) A method for isolating a tetrameric form of uricase from a solution of uricase, said solution comprising tetrameric uricase and uricase aggregates, comprising the steps of:

applying said solution to at least one separation column at a pH between about 9 and 10.5; and

recovering from said column one or more fractions that contain isolated tetrameric uricase, wherein said one or more fractions are substantially free of uricase aggregates.

43. (NEW) The method of Claim 42, wherein said solution of said uricase is applied to said column at a pH of 10.2.

44. (NEW) The method of Claim 42, wherein said separation is based on a property selected from the group consisting of ion exchange and size exclusion.

45. (NEW) The method of Claim 42, further comprising the step of analyzing said fractions to determine at least one property selected from the group consisting of the presence of said tetrameric uricase and the absence of uricase aggregates.

46. (NEW) The method of Claim 45, wherein said analyzing step comprises at least one analysis selected from the group consisting of chromatography, centrifugation, light scattering and electrophoresis.

47. (NEW) The method of Claim 46, wherein said chromatography is high performance liquid chromatography.

48. (NEW) The method of Claim 42, wherein said isolated tetrameric uricase contains less than about 10% uricase aggregates.

49. (NEW) An isolated tetrameric uricase produced by the method of Claim 42.

50. (NEW) The isolated tetrameric uricase of Claim 49, wherein the uricase is a mammalian uricase.

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51. (NEW) The isolated tetrameric uricase of Claim 50, wherein the uricase is porcine liver, bovine liver or ovine liver uricase.

52. (NEW) The isolated tetrameric uricase of Claim 49, wherein the uricase is recombinant.

53. (NEW) The isolated tetrameric uricase of Claim 52, wherein the uricase has substantially the sequence of porcine, bovine, ovine or baboon liver uricase.

54. (NEW) The isolated tetrameric uricase of Claim 52, wherein the uricase is chimeric.

55. (NEW) The isolated tetrameric uricase of Claim 54, wherein the chimeric uricase contains portions of porcine liver and baboon liver uricases.

56. (NEW) The isolated tetrameric uricase of Claim 55, wherein the chimeric uricase is pig-baboon chimeric uricase.

57. (NEW) The isolated tetrameric uricase of Claim 55, wherein the chimeric uricase is porcine uricase containing lysine in place of arginine at residue number 291 and serine in place of threonine at residue number 301.

58. (NEW) The isolated tetrameric uricase of Claim 52, wherein the uricase has substantially the sequence of baboon liver uricase in which tyrosine 97 has been replaced by histidine.

59. (NEW) The isolated tetrameric uricase of Claim 52, wherein the uricase comprises an amino terminal and a carboxyl terminal, and wherein the uricase is truncated at one terminal or both terminals.

60. (NEW) The isolated tetrameric uricase of Claim 49, wherein the uricase is a fungal or microbial uricase.

61. (NEW) The isolated tetrameric uricase of Claim 60, wherein the fungal or microbial uricase is isolated from *Aspergillus flavus*, *Arthrobacter globiformis*, *Bacillus sp.*, or *Candida utilis*, or is a recombinant enzyme having substantially the sequence of one of those uricases.

62. (NEW) The isolated tetrameric uricase of Claim 49, wherein the uricase is an invertebrate uricase.

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63. (NEW) The isolated tetrameric uricase of Claim 62, wherein the invertebrate uricase is isolated from *Drosophila melanogaster* or *Drosophila pseudoobscura*, or is a recombinant enzyme having substantially the sequence of one of those uricases.

64. (NEW) The isolated tetrameric uricase of Claim 49, wherein the uricase is a plant uricase.

65. (NEW) The isolated tetrameric uricase of Claim 64, wherein the plant uricase is isolated from root nodules of *Glycine max* or is a recombinant enzyme having substantially the sequence of that uricase.

66. (NEW) The isolated tetrameric uricase of Claim 49, each subunit of the uricase being subsequently covalently linked to an average of 2 to 10 strands of PEG to form a PEG-uricase conjugate, wherein each molecule of PEG has a molecular weight between about 5 kDa and 100 kDa, and wherein the conjugate retains at least about 75% of the uricolytic activity of unconjugated uricase and is substantially non-immunogenic.

67. (NEW) The isolated tetrameric uricase of Claim 66, wherein the PEG has an average molecular weight between about 10 kDa and 60 kDa.

68. (NEW) The isolated tetrameric uricase of Claim 67, wherein the PEG has an average molecular weight between about 20 kDa and 40 kDa.

69. (NEW) The isolated tetrameric uricase of Claim 66, wherein the average number of covalently coupled strands of PEG is 3 to 8 strands per uricase subunit.

70. (NEW) The isolated tetrameric uricase of Claim 69, wherein the average number of covalently coupled strands of PEG is 4 to 6 strands per uricase subunit.

71. (NEW) The isolated tetrameric uricase of Claim 66, wherein the strands of PEG are covalently coupled to uricase via linkages selected from the group consisting of urethane linkages, secondary amine linkages, and amide linkages.

72. (NEW) The isolated tetrameric uricase of Claim 66, wherein the PEG is linear.

73. (NEW) The isolated tetrameric uricase of Claim 66, wherein the PEG is branched.

74. (NEW) A pharmaceutical composition for lowering uric acid levels in a body fluid or tissue, comprising the isolated tetrameric uricase of Claim 49 and a pharmaceutically acceptable carrier.